

**REMARKS**

The present application contains claims 1-173, the status of which is as follows:

(a) Claims 2, 10-12, 16-17, 20, 22, 49-50, 54, 64-66, 68-69, 82-86, 88-93, 96, 105-107, 110, 112, 114-118, 121, and 123-126 are as originally filed.

(b) Claims 100-101 were previously presented.

(c) Claims 1, 3-7, 13-15, 18-19, 21, 26-27, 36, 41-44, 48, 51-53, 55-59, 61-63, 67, 70, 79-81, 87, 94-95, 97-99, 102-104, 108-109, 111, 113, 119-120, 122, and 127-130 have been currently amended.

(d) Claims 8-9, 23-25, 28-35, 37-40, 45-47, 60, 71-78, have been cancelled without prejudice.

(e) Claims 131-173 were previously withdrawn.

The Applicant thanks Examiners Maewall and Gollamudi for the courtesy of an interview with the Applicant's representative, Sanford T. Colb (Reg. No. 26,856) on January 8, 2008. It was proposed by Mr. Colb that, although not believed necessary for patentability, the claims be amended to recite a self-expansible capsule that expands to improve contact between an electrode on the capsule and the wall of the gastrointestinal tract, and which drives a current through the electrode that is configured to form openings in tight junctions of the epithelial layer of a subject's gastrointestinal tract. The examiners said that they will consider the proposed amendments and carry out a new search.

Independent claim 1 has been amended:

1) to recite "a pH-sensitive coating" instead of "an environmentally sensitive mechanism"

2) to recite "an electrode" and "a control component... adapted to facilitate passage of the drug through an epithelial layer of the gastrointestinal tract by forming openings in tight junctions of the epithelial layer by driving a current into a wall of the gastrointestinal tract," instead of a "driving mechanism," and

3) to recite "a self-expansible portion having the first electrode thereon, and configured to improve contact between the gastrointestinal tract wall and the electrode by expanding the portion."

The pH-sensitive coating finds support in the specification. For example paragraph [0061] of the application as published (US Patent Application Publication 2004/0253304) states:

In some embodiments of the present invention, the drug-delivery system comprises a mechanism that is operative to be responsive to its environment, such as, for example, a pH-sensitive coating. The coating is typically configured, using techniques known in the art, to dissolve upon entering a small intestine of a patient.

Additionally, claims 23 and 24 as filed recite:

23. The apparatus according to claim 1, wherein the environmentally-sensitive mechanism comprises a coating on a surface of the capsule.

24. The apparatus according to claim 23, wherein the coating comprises a pH-sensitive coating.

The functionality of the electrode and the control component find support in paragraphs [0206] and [0353] of the '304 publication:

[0206] In an embodiment, the control component is adapted to configure the current to increase conduction of the drug through tight junctions of the endothelial layer of the gastrointestinal tract by means of electropulsation.

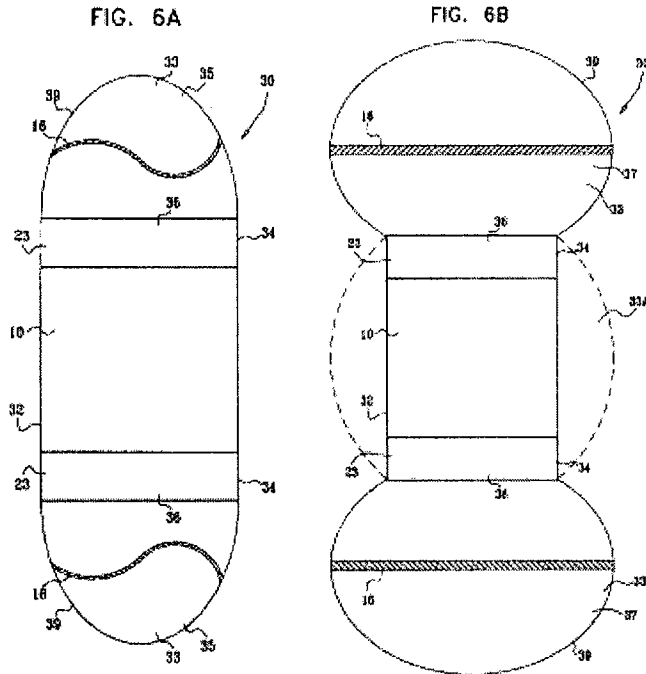
[0353] In accordance with some embodiments of the present invention, the electrotransport may include any one of, or a combination of, iontophoresis, electroosmosis, and electrophoresis, which enhance diffusion processes through the epithelial cells, and, for some applications, additionally electroporation, **which physically punctures or opens biological barriers, along the tight junctions of the epithelial cell boundaries, enabling passage of large molecules through the epithelium.**

The language of "control component" in this context is found, for example, in claims 58 and 59 as filed.

Support for the self-expansible portion can be found in Paragraph [0358] of the '304 publication:

[0358] FIGS. 6A and 6B illustrate ingestible, electrically-assisted, drug-delivery system 30 in respective resting and drug-delivery phases thereof, in accordance with an embodiment of the present invention. In this embodiment, device 10 comprises self-expansible portions 33, enclosed in a biologically-inert and biocompatible elastic film 39, such as natural or synthetic thin rubber. For some applications, electrodes 16 are painted on elastic film 39, for better

contact between electrodes 16 and the GI walls. The self-expansible effect may be produced, for example, by a chemical reaction of a substance 35 (FIG. 6A), that produces a gas 37, such as CO<sub>2</sub> (FIG. 6B).



Paragraph 129 of the specification also notes: "In an embodiment, the self-expansible portion is adapted to expand responsive to an inflow of fluid from the gastrointestinal tract."

Parallel amendments have been made to independent claims 129 and 130.

Claims 3-7, 13-15, 18-19, 21, 26-27, 36, 41-44, 48, 51-53, 55-59, 61-63, 67, 70, 79-81, 87, 94-95, 97-99, 102-104, 108-109, 111, 113, 119-120, 122, and 127-128 have been currently amended to conform with the amendments made to independent claim 1.

No new matter has been added. Reconsideration is respectfully requested.

### ***Rejections under 35 U.S.C. 112***

Claims 1-130 were rejected under 35 U.S.C. 112 first and second paragraphs. Claim 1 recited an "environmentally sensitive mechanism" and a "driving mechanism." These claims are currently amended, and the rejections are moot in light of the amendments. The Applicant in any case chooses to respond here to the Examiner's rejections of these claims. The Examiner argued that these elements were not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Furthermore, the Examiner asserted that claim 1 was indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as his invention. The Applicant respectfully submits that a person of ordinary skill in the art who has read the specification would understand meaning of the environmentally sensitive mechanism and the driving mechanism, as multiple examples of both mechanisms were described in the specification. The Applicant further submits that the person of ordinary skill in the art would believe that the Applicant indeed had possession of the invention at the time of filing, based on the many examples of suitable embodiments. Also, regarding the Examiner's comments that claim 1 does not recite any structural limitations (these comments being moot in light of the current amendments), the Applicant notes that MPEP 2173.05(g) states that "a functional limitation is an attempt to define something by what it does, rather than by what it is (e.g., as evidenced by its specific structure or specific ingredients). There is nothing inherently wrong with defining some part of an invention in functional terms."

As noted, although the Applicant disagrees with the 35 USC 112 rejections, independent claims 1, 129 and 130 have been amended:

1) to recite "a pH-sensitive coating" instead of "an environmentally sensitive mechanism," and

2) to recite "an electrode" and "a control component... adapted to facilitate passage of the drug through an epithelial layer of the gastrointestinal tract by forming openings in tight junctions of the epithelial layer by driving a current into a wall of the gastrointestinal tract," instead of a "driving mechanism."

The amended claims are supported in the text of the specification, as described hereinabove. Furthermore, the amended claims particularly point out and distinctly claim the subject matter which the Applicant regards as his invention.

### ***Rejections under 35 U.S.C. 103***

Claims 1-130 were rejected by the examiner under 35 U.S.C. 103(a) as being unpatentable over GB 2374149A to Thomas in view of the combination of references of US 6,453,199 to Kobozev, US 5,925,030 to Gross, PCT Publication WO 02/098501 to Yona KEISARI, and "Iontophoresis-enhanced absorptive flux of polar molecules across intestinal tissue in vitro," by Leonard.

The Thomas patent describes a swallowable intra-body drug dispensing capsule comprising a sensing module, a bio-active substance dispenser and a component including memory and logic. As stated by the Examiner on page 7 of the Office Action

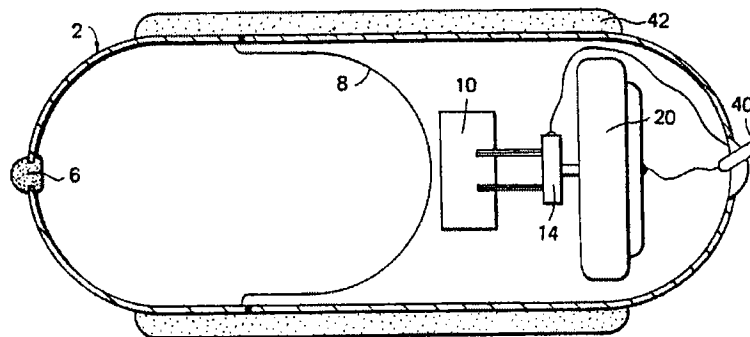
dated 18 October, 2007, "Thomas does not teach [a] driving mechanism comprising electrodes, control units, etc."

The Kobozev patent describes an electrical gastro-intestinal tract stimulator comprising a casing with electrodes and in the form of a medicinal capsule containing a power source, a control unit of which M outputs are connected to M electrodes, a device for receiving signals from internal organs and/or an external transmitter, to (1-N) outputs of which are connected (1-N) inputs of the control unit. The stimulation of the stimulator is intended to be therapeutic in and of itself, and the patent as a whole lacks any significant reference to administration of drugs. The control unit of the Kobozev stimulator is not adapted to form openings in tight junctions of the epithelial layer of a subject's gastrointestinal tract. Furthermore, as the Examiner states on page 8 of the Office Action "Kobozev does not teach [a] self-expansible portion."

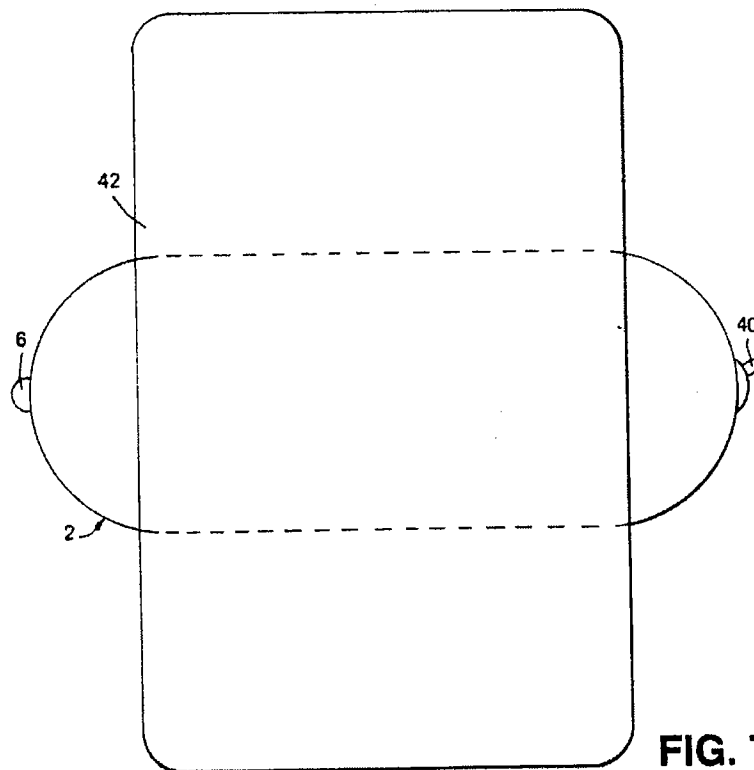
Claims 13-22, as previously pending, recited a self-expansible portion. US Patent 5,925,030 to Yossi Gross was cited in the Office Action against claims that recite a self-expansible portion. In embodiments of the '030 patent, a capsule comprises a gas chamber and a drug delivery chamber, which are separated by a membrane. Gas is generated in the gas chamber, which increases pressure in the gas chamber and pushes the membrane in the direction of the drug delivery chamber causing the drug delivery chamber to contract. Contraction of the drug delivery chamber expels a drug-containing liquid through an opening in the drug delivery chamber. If the Examiner's intention was that the gas chamber is a self-expansible portion, then the claims as currently amended would not read upon or be obvious in light of the '030 patent, since the claims as currently amended recite "a self-expansible portion **having the first electrode thereon, and configured to improve contact between a gastrointestinal tract wall and the electrode by expanding the portion.**"

In addition, the Applicant notes that the Background section of the '030 patent describes PCT Publication WO 94/01165 to Joseph Gross (who is the same person as the Yossi Gross who is an inventor of the present patent application). The Gross PCT Publication explicitly discloses a self-expansible portion on a capsule. Figures 6 and 7 of the '165 application (shown below) schematically illustrate an embodiment of a drug delivery capsule that comprises a water-swellaable portion 42 in contracted (Fig. 6) and expanded (Fig. 7) states. The purpose of the water-swellaable portion is to control the residence time of the device in the subject's body cavity, as stated in the final paragraph of Page 7 of the '165 application. The claims as currently amended do not read upon and are not obvious in light of the '165 application, since the claims as currently amended recite "a self-expansible portion **having the first electrode thereon, and**

**configured to improve contact between a gastrointestinal tract wall and the electrode by expanding the portion."**



**FIG. 6**



**FIG. 7**

Furthermore, the device described in the Gross PCT Publication is not adapted to form openings in tight junctions of the epithelial layer of a subject's gastrointestinal tract.

PCT Publication WO 02/098501 to Yona Keisari describes a method of treating tumor tissue of an individual by applying to cells of the tumor electrical field pulses with electrodes. The pulses are adapted to induce endocytosis-mediated cell death, and are

not adapted to form openings in tight junctions between the cells. Furthermore, the '501 application does not teach applying the pulses from a swallowable capsule. Furthermore, the '501 application does not teach or suggest putting electrodes on a self-expandable portion of a swallowable capsule.

The Leonard article describes the use of iontophoresis to increase drug passage through the epithelial lining of the gastrointestinal tract. Iontophoresis is not the invention recited in currently amended claims 1, 129, and 130. The apparatus of the currently amended independent claims increases absorption by forming openings in the tight junctions of the epithelial layer. Iontophoresis is a method for pushing a drug through a surface, and is clearly distinguished, in the specification of the current application, from the invention as recited in the independent claims of the present patent application.

***Rejections for double patenting***

Claims 1-130 were provisionally rejected on the ground of non-statutory obviousness-type double patenting, over US 10/901,742, 11/579,246, and 10/838,072. While not necessarily agreeing with the basis for these rejections, the Applicant is filing terminal disclaimers herewith.

The Applicant believes the amendments and remarks presented hereinabove to be fully responsive to all of the grounds of rejection and objection raised by the Examiner. In view of these amendments and remarks, the Applicant respectfully submits that all of the claims in the present application are now in order for allowance. Notice to this effect is respectfully requested.

Respectfully submitted,

RatnerPrestia



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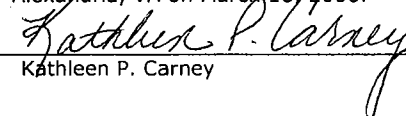
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I hereby certify that this correspondence is being electronically transmitted to: Commissioner for Patents, Alexandria, VA on March 18, 2008.



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